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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,477	08/04/2003	Paul Lehmann	21368	8405

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HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY, NJ 07110

EXAMINER

ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
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1656

DATE MAILED: 09/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/634,477

Applicant(s)

LEHMANN ET AL.

Examiner

Hope A. Robinson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-15 is/are rejected.
- 7) ☒ Claim(s) 2 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 August 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/30/03; 3/3/04; 3/15/04; 6/21/04</u> | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Application Status

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

2. Claims 1-15 are pending and are under examination.

Specification

3. The specification is objected to because of the following informalities:

The specification is objected to because on page 1, the priority information is not provided, for example, "This application claims foreign priority to EP 02019100.3, filed August 29, 2002".

Drawing

4. The drawings are objected to because Figure 1 has a sequence, however, no sequence identifier is present. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of

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the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance. Applicant is reminded to file Formal Drawings.

Information Disclosure Statement

5. The Information Disclosure Statement filed on October 30, 2002, March 3, 2004, March 15, 2004, March 21, 2004 and February 13, 2004 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

Claim Objection

6. Claims 2 and 8 are objected to because of the following informalities:

Claim 2 is objected to because the claim depends from a rejected base claim.

Claim 8 is objected to because the claim is missing the article "a" on line 10, where the claim recites "wherein R is lower-alkyl" which should be " wherein R is a lower-alkyl".

Correction is required.

Claim Rejections - 35 USC § 112

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 8-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a method of treating disturbances in iron distribution by administering human erythropoietin, wherein the erythropoietin protein is a conjugate, said conjugate comprising an erythropoietin protein having at least one free amino group and having the *in vivo* biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells and selected from the group consisting of human erythropoietin and analogs thereof ...", thus the claims encompass fragments. The specification does not demonstrate retention of function for the fragments to demonstrate possession of the genus as claimed in the invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. See *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997). Additionally, the specification fails to provide any additional representative species of

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the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described, are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In addition, the claims are directed to a pharmaceutical compositions (see claims 13-15), however, the claims do not recite a pharmaceutically acceptable carrier or excipient, thus, the claimed invention lacks adequate written description as the composition requires a carrier.

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 3-15 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claims 3-15 lack clear antecedent basis for "the erythropoietin protein" claim 1 recites "human erythropoietin".

Claims 8 and 11 lacks clear antecedent basis as the claims recite "the erythropoietin protein is a conjugate" and independent claim 1 recites, "human erythropoietin", thus there is no recitation of "protein" or "conjugate". Claims 8 and 11 also lack clear antecedent basis for the recitation of "an erythropoietin protein" because this language reads on more than one protein and fragments, which has no basis in claim 1.

Claims 13-15 are indefinite because the claims recite a pharmaceutical composition, however, the composition does not have a carrier.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

10. Claim 1, 3-12 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Bosman et al. (Diabetes Care, vol. 24, pages 495-499, 2001) in view HOFFMANN-LA ROCHE (EP 1064 951, January 3, 2001 (cited on IDS - October 3, 2003)).

Bosman et al. disclose the relatedness between erythropoietin deficiency and anemia in patients suffering from early diabetic nephropathy. The reference performed studies of patients, which determined that anemia associated with EPO deficiency occurs early in diabetes (see page 495). As the reference by Bosman et al. teach erythropoietin, claims reciting epoetin alfa or beta and darbepoetin are obvious as these are properties of erythropoietin. Therefore, one of ordinary skill in the art can conclude that administration of erythropoietin to the patients in the study of Bosman et al. would result in treatment of iron disturbances (anemia) in these patients suffering from diabetic nephropathy. Bosman et al. does not teach a modification in the protein of 1 to 6 glycosylation site or pegylation. However, HOFFMANN-LA ROCHE teach glycosylation of erythropoietin (see page 2 of the reference); and pegylated erythropoietin conjugates and the chemical structures claimed (see claim 4 and 7-15, pages 1-5 of the reference).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have a method of treating disturbances in iron in a patient suffering from diabetes comprising administering human erythropoietin because Bosman et al. teach a study comprising erythropoietin deficiency in patients suffering from diabetes and

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concluded that anemia presented in these patients, thus the administration of erythropoietin would result in treatment of anemia (iron disturbance) in patients suffering from diabetes. In addition, HOFFMANN-LA ROCHE teach a glycosylated, pegylated and conjugated erythropoietin, and the chemical structures claimed in the instant invention. One of ordinary skill in the art would be motivated to combine the teachings of the references because erythropoietin is known in the art to treat anemia (iron disturbance) in patients and the art teaches that early treatment with erythropoietin in diabetic patients results in slow onset of diabetic retinopathy and macular edema. Further, HOFFMANN-LA ROCHE teach erythropoietin for the same purpose and that as a conjugate to PEG an increased half-life is achieved. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

Basis For NonStatutory Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1 and 3-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-14 of copending Application No. 10/706,701. An obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). *See In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The copending application claim 1 is directed to a method of treating disturbances in iron distribution in a patient suffering from heart disease comprising administering a therapeutically effective amount of human erythropoietin. The dependent claims hereto are directed to an erythropoietin that is epoetin alfa or beta (claim 3); SEQ ID NO:1 (claim 4); a modification of 1 to 6 glycosylation sites (claim 5); a darbepoetin (claim 6); pegylated (claim 7); and a conjugate having a particular structure as set forth in claims 8-14. The instant application claim 1 is directed to a method of treating disturbances in iron distribution in a patient suffering from

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diabetes comprising administering a therapeutically effective amount of human erythropoietin.

The dependent claims hereto are directed to an erythropoietin that is epoetin alfa or beta (claim 3); SEQ ID NO:1 (claim 4); a modification of 1 to 6 glycosylation sites (claim 5); a darbepoetin (claim 6); pegylated (claim 7); and a conjugate having a particular structure as set forth in claims 8-12. The copending application claims differ from the instant application in that the patient is suffering from heart disease, whereas the instant application patient is suffering from diabetes, however, the methods have one step, administering erythropoietin, thus the resulting effect will be the same. Moreover, the art generally recognizes that heart disease is a risk with diabetes, for example type II diabetes. In fact, studies have shown that there is a five fold increase in the risk for heart disease in women with diabetes, thus the administration of erythropoietin is critical to both diseases claimed in the applications. Therefore, the two sets of claims differ in scope but are obvious one over the other, as the intended use does not materially change the composition administered.

13. Claims 1 and 3-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4-15 of copending Application No. 11/013,560. An obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). *See In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir.

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1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant application claim 1 is directed to a method of treating disturbances in iron distribution in a patient suffering from diabetes comprising administering a therapeutically effective amount of human erythropoietin. The dependent claims hereto are directed to an erythropoietin that is epoetin alfa or beta (claim 3); SEQ ID NO:1 (claim 4); a modification of 1 to 6 glycosylation sites (claim 5); a darbepoetin (claim 6); pegylated (claim 7); and a conjugate having a particular structure as set forth in claims 8-12. The copending application claim 1 is directed to a method of treating disturbances in iron distribution in a patient suffering from chronic inflammatory intestinal disease comprising administering a therapeutically effective amount of human erythropoietin. The dependent claims hereto are directed to an erythropoietin that is epoetin alfa or beta (claim 4); SEQ ID NO:1 (claim 5); a modification of 1 to 6 glycosylation sites (claim 6); a darbepoetin (claim 7); pegylated (claim 8); and a conjugate having a particular structure as set forth in claims 9-15. The instant application claims differ from the copending application in that the patient is suffering from diabetes, whereas the copending application patient is suffering from chronic inflammatory intestinal disease, however, the methods have one step, administering erythropoietin, thus the resulting effect will be the same. Thus, the two sets of claims differ in scope but are obvious one over the other, as the intended use does not materially change the composition administered.

Conclusion

14. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner

HR 8/30/05
HOPE ROBINSON
PATENT EXAMINER